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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,116	11/16/2005	Amiram Grinvald	U 015800-7	8078

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EXAMINER	
FERNANDEZ, KATHERINE L	
ART UNIT	PAPER NUMBER
3768	

NOTIFICATION DATE	DELIVERY MODE
11/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/537,116	GRINVALD ET AL.	
	Examiner	Art Unit	
	KATHERINE L. FERNANDEZ	3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-56,58 and 66-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-56,58 and 66-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 45-53, 66-77, 79-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grinvald et al. (WO 99/63882) as cited by applicant in view of Wong et al. ("Retinal microvascular abnormalities and incident stroke: the Athersclerosis Risk in Communities Study", October 2001) as cited by applicant and further in view of Owsley (US Patent No. 5,727,561).

Grinvald et al. disclose a method for vascular analysis of a subject, comprising the steps of: optically imaging moving erythrocytes within at least one optically accessible blood vessel of a subject (pg. 3, last paragraph-pg. 4, top paragraph; pg. 5; pg. 8, 1st-2nd paragraphs); determining from said optical imaging at least one flow characteristic of said erythrocytes in at least one optically accessible blood vessel (pg. 5; pg. 9, 5th paragraph-pg. 10, 1st paragraph; pg. 12, 3rd paragraph, referring to determining blood flow direction and a rate-of-flow map from data from images) and generating an output on an output device (pg. 5). The blood vessel can be a retinal blood vessel or can be located in tissue of an internal organ (i.e. brain tissue) (pg. 7, last paragraph-pg. 8, first paragraph). The optical imaging comprises acquiring at least two sequential images of erythrocytes in said at least one optically accessible blood vessel (pg. 3, last paragraph-pg. 4, 2nd paragraph; pg. 5, last paragraph). Grinvald et al.

further disclose a system for performing the method discussed above, which includes a light source for illuminating at least one optically accessible blood vessel of the subject (pg. 6, 3rd paragraph), an imager for acquiring a plurality of images of moving erythrocytes showing sequential spatial distribution of said moving erythrocytes in said at least one optically (pg. 5), an image discriminator for determining from said plurality of images showing sequential spatial distribution, a flow pattern of erythrocytes along said blood vessel (pg. 5; pg. 9, last paragraph-pg. 10, 2nd paragraph), and a flow analyzer for analyzing said flow pattern to determine at least one flow characteristic of erythrocytes along said at least one optically accessible blood vessel of the subject (pg. 5; pg. 11, 2nd paragraph; pg. 12, 3rd-4th paragraph). Their system further comprises a wavelength selector (i.e. bandpass filter) configured to configure said imager to acquire said images of said at least one optically accessible blood vessel over a limited wavelength band (pg. 6, last paragraph). The wavelength selector is located in an illuminating pathway between said light source and said at least one optically accessible blood vessel and in an imaging pathway between said at least one optically accessible blood vessel and said imager (pg. 6, last paragraph). Although Grinvald et al. do not specifically disclose that the wavelength band is between 2 and 30 nm, it would have been within the skill of one of ordinary skill in the art to modify the invention of Grinvald et al. to experimentally adjust the wavelength band to between 2 and 30 nm in order to determine the appropriate wavelength. The light source for illuminating said at least one optically accessible blood vessel of the subject is a pulsed source having a pulse to pulse interval of less than 1 second or between 5 and 200 ms (pg. 5, last paragraph-pg.

6, 3rd paragraph). Grinvald et al. further disclose that their system includes a computer and a display monitor for viewing the results of automatic image analysis and permitting interactive image analysis, and a printer for hard copy output of analysis results (pg. 5).

However, they do not specifically disclose that their method includes the step of utilizing said at least one flow characteristic for identifying roughness on an inner wall of said at least one optically accessible blood vessel or that their invention includes a wall analyzer for utilizing said at least one flow characteristic for determining at least one property of an inner surface wall of said blood vessel. With regards to claims 51-52 and 68-69, Grinvald et al. do not specifically disclose that their method includes the step of utilizing said identifying of said roughness on said inner wall of said at least one optically accessible blood vessel in order to determine a level of arteriosclerosis in the subject. Further, they do not specifically disclose that their method further comprises the step of utilizing said identifying of said roughness on said inner wall of said at least one optically accessible blood vessel in order to determine a condition of another blood vessel of the subject.

Wong et al. disclose a study investigating the relation between retinal microvascular abnormalities to incident stroke (pg. 1134, left column, Summary:Background). They conclude that retinal microvascular lesions (i.e. roughness on wall of blood vessel) can be markers of general vascular pathology (such as atherosclerosis, which is a form of arteriosclerosis) rather than specific microvascular pathology (pg. 1139, left column, 1st paragraph). At the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the invention of Grinvald

et al. to include identifying roughness in an inner wall of said at least one optically accessible blood vessel and include the limitations of claims 51-52 and 68-69, as taught by Wong et al., in order to provide a non-invasive way of determining the risk of arteriosclerosis in an individual (pg. 1139, left column, 1st paragraph).

However, the above combined references do not specifically disclose that roughness is identified by utilizing said at least one flow characteristic or that their invention includes a wall analyzer for utilizing said at least one flow characteristic for determining at least one property of an inner surface wall of said blood vessel.

Owsley discloses an apparatus and method for non-invasive detection and analysis of turbulent blood flowing in blood vessels (column 1, lines 15-18). They disclose that it is well known that turbulent blood flow in one or more vessels in an individual often indicates the presence of arterial diseases or defects, that is, the detection of turbulent blood flow within a patient's blood vessels can serve as a primary diagnostic indicator of occlustic, aneurystic, thrombotic and other vascular conditions (column 1, lines 21-26). They disclose that a vessel with an arterial occlusion (32) (i.e. plaque buildup on an inner wall of vessel) transforms normal laminar blood flow to a chaotic, turbulent flow (i.e. turbulent flow indicative of roughness on an inner wall of vessel) (column 4, lines 17-36; see Figure 1). A processing module receives the detected signals and detects the existence of turbulent flow, locates the position of turbulent flow and enables the detection of arterial defects in relatively early stages of a disease or other abnormality (column 4, lines 36-50; column 9, lines 31-38). Note that in Figure 1, turbulent flow (26) is identified as a change the direction and rate of blood

flow. At the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the invention of Grinvald et al. to have their computer serve as a wall analyzer to perform the step of utilizing at least one flow characteristic (i.e. flow direction, flow rate) for identifying roughness on an inner wall of said at least one optically accessible blood vessel, as Owsley teaches that flow characteristics (i.e. turbulent flow, flow direction, flow rate) are indicators of plaque formation (i.e. roughness on inner wall of blood vessel), thus enabling earlier diagnosis of a disease (column 1, line 62-column 2, line 4).

3. Claims 54-56 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grinvald et al. in view of Wong et al. and Owsley and further in view of Taylor '02 ("In Vivo Quantification of Blood Flow and Wall Shear Stress in the Human Abdominal Aorta During Lower Limb Exercise", March 2002).

As discussed above, the above combined references meet most of the limitations of claim 54 (i.e. optically imaging moving erythrocytes once and then again, determining from said optical imaging at least one erythrocytic flow characteristic, and utilizing differences in said at least one flow characteristic to determine a roughness index of an inner wall of said at least one optically accessible blood vessel). However, they do not specifically disclose that optically imaging the moving erythrocytes the first time is performed with subject having a first blood pressure, said first pressure being subject to change to a second blood pressure, optically imaging the moving erythrocytes within the blood vessel again when said first blood pressure of said subject has changed to said second blood pressure, nor do they disclose that the change from said first blood

pressure to said second blood pressure is caused by at least one of exercise and drugs administered to the subject. They also do not disclose that the change of said first blood pressure to said second blood pressure is a result of the subject's heartbeat. Further, they do not disclose that their method includes the limitations of instant claims 56 and 58, which disclose that the first blood pressure corresponds to a first point in a cardiac cycle of the subject wherein said second blood pressure corresponds to a second point in the cardiac cycle of the subject, and wherein the optical imaging steps comprise optically imaging moving erythrocytes within said at least one optically accessible blood vessel when the subject's cardiac cycle is respectively at said first and second points in the subject's cardiac cycle, or that the optical imaging steps comprise detecting a parameter of the subject selected from the group consisting of the subject's cardiac cycle and blood pressure of the subject, and optically imaging the moving erythrocytes in response to the selected parameter.

Taylor '02 disclose a study that measures, in vivo, the spatial distribution of blood flow velocities in the abdominal aorta of human subjects during upright rest and light exercise conditions (pg. 403, left column, 3rd paragraph). They disclose that data was collected at rest and during steady-state exercise conditions within the range of light exercises (i.e. data was collected at two different heart rates, which cause a change in blood pressure; also scans were synchronized with the subject's heart beat) (pg. 403, right column, 2nd paragraph). They further disclose that the image acquisitions were gated to the cardiac cycle using a plethysmograph, and that the data was retrospectively reconstructed at 16 discrete time points within the cardiac cycle (pg. 403,

right column, 3rd paragraph). Further, the subjects monitored their own heart rate, which was displayed in real-time on a pulse monitor (pg. 403, right column, 2nd paragraph). At the time of the invention, it would have been obvious to one of ordinary skill in the art to have the optical imaging steps in the method of the above combined references be performed at different blood pressure readings, wherein the change in pressure readings is a result of exercise performed by the subject and to further include the limitations of claims 56 and 58, as taught by Taylor '02, in order to determine the effect of activities that change blood pressure (such as exercise) have on flow characteristics (pg. 403, left column, 2nd-3rd paragraphs).

4. Claim 78 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grinvald et al. in view of Wong et al. and Owsley as applied to claim 66 above, and further in view of Flower '94 (US Patent No. 5,279,298).

As discussed above, the above combined references meet the limitations of claim 66. Further, they disclose that the imager is configured to acquire images at predetermined intervals (see Grinvald, pg. 5, last paragraph-pg. 6, 2nd paragraph). However, they do not specifically disclose that the light source for illuminating said at least one optically accessible blood vessel of the subject is a continuous source. Flower '94 discloses a method and apparatus to detect and treat neovascular membranes in the ocular vasculature of the fundus of the eye (column 1, lines 8-10). They disclose the use of a continuous light source and that the imager acquires the images at predetermined intervals (column 5, lines 34-52, referring to the computer recording successive images or frames of the fundus of the eye with the passage of

time). At the time of the invention, it would have been obvious to one of ordinary skill in the art to include the above limitations in the system of the above combined references, as their invention requires an illumination source and Flower et al. teach the successful use of a continuous illumination source when imaging a vessel.

Response to Arguments

5. Applicant's arguments with respect to claims 45-56,58 and 66-81 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE L. FERNANDEZ whose telephone number is (571)272-1957. The examiner can normally be reached on 8:30-5, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric F Winakur/
Primary Examiner, Art Unit 3768